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Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted
a patent (Rule 4.17(ii)) for the following designations AE,
AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,
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MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC,
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MR, NE, SN, TD, TG)

— as to the applicant's entitlement to claim the priority of the
earlier application (Rule 4.17(iii)) for the following design-
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BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC,
EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
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Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: CRYSTAL STRUCTURES OF JNK-INHIBITOR COMPLEXES AND BINDING POCKETS THEREOF

(57) Abstract: The invention relates to crystalline molecules or molecular complexes that comprise binding pockets of c-Jun N-terminal kinase 3 (JNK3) or its homologues. The invention also relates to crystals comprising JNK3 and an inhibitor. The present invention also relates to a computer comprising a data storage medium encoded with the structural coordinates of JNK3 binding pockets and methods of using a computer to evaluate the ability of a compound to bind to the molecule or molecular complex. This invention also relates to methods of using the structure coordinates to solve the structure of homologous proteins or protein complexes. In addition, this invention relates to methods of using the structure coordinates to screen for, design and optimize compounds, including agonists and antagonists, which bind to JNK3 or homologues thereof.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/00899

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G06F 19/00; A01N 61/00

US CL : 702/27, 514/1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 702/27, 514/1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	XIE et al. Crystal Structure of JNK3: a kinase implicated in neuronal apoptosis. Structure. August 1998, Volume 6, pages 983-991, especially see page 983, Results and Conclusions Sections; page 985, Figure 2; page 986, The phosphorylation lip section and Figure 3; page 989, column 2, lines 9-17; and page 990, Table 1.	1 and 3-6
A	US 6,162,613 A (SU et al.) 19 December 2000 (19.12.2000), column 6, lines 58-64; column 7, lines 1-67 to column 8, lines 1-48; and claim 1.	24-28
A	DRENTH, J. Principles of Protein X-ray Crystallography, 1995, Springer-Verlag, page 16.	1-6 and 24-28
A,P	SERVICE, R.F. Tapping DNA for Structures Produces a Trickle: News Focus. Science. 01 November 2002, Volume 298, Pages 948-950.	1-6 and 24-28

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/00899

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: Group I, claims 1-7 and Group V, claims 24-28, First specie.
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐
☐

- The additional search fees were accompanied by the applicant's protest.
No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/US03/00899

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-7, drawn to a crystal comprising a JNK3 protein and an inhibitor.

Group II, claim(s) 8 and 9, drawn to a method of producing a JNK3-inhibitor complex crystal.

Group III, claim(s) 10-22, drawn to a crystalline molecule or molecular complex and a computer comprising the data directed to the said crystalline molecule or molecular complex.

Group IV, claim(s) 23, drawn to a method for designing, selecting and/or optimizing a chemical entity that binds to a molecular complex.

Group V, claim(s) 24-28, drawn to a method for evaluating the ability of a chemical entity to associate with a molecule or molecular complex.

Group VI, claim(s) 29, drawn to a method for identifying an agonist or antagonist of a molecule or molecular complex.

Group VII, claim(s) 30-32, drawn to a method of utilizing molecular replacement to obtain a structural model of a molecule or a molecular complex of unknown structure.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

Groups I-VII are directed 5 species of inhibitors listed in claim 2.

According to PCT Rule 13.2 and to the guidelines in Section (f)(i)(A) of Annex B of the PCT Administrative Instructions, all alternatives of a Markush Group must have a common property or activity. Although the chemical compounds of claim 2 share a common feature of an inhibitor, the compounds are not regarded as being of similar nature because all the alternatives do not share a common property or activity. Each substrate inhibitor is identified by its physical and chemical properties and the physical and chemical properties dictate their binding activity. Therefore, the physical and chemical properties of each inhibitor do not provide for a common property or activity or a significant structural element.

For the invention of Group I, the first specie is the first inhibitor, (N-[4-(5-Methyl...)-acetamide, listed in claim 2. For each additional group, the fee would be \$210.00. For each additional species per group thereafter, the fee would be \$210.00. Then, the cost all the groups and all of the species would be \$7140.00.